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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 01/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/382,837	BORODIC, GARY E.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/25/04, 6/3/04, and 10/25/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-8,10-12,17-19 and 21-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-8,10-12,17-19 and 21-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 3/25/04 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendments and remarks, filed 3/25/04, 6/03/04, and the election of species, filed 10/25/04, have been entered.

2. Upon reconsideration, the species requirement has been withdrawn.

3. Claims 1, 3, 5-8, 10-12, 17-19, 21-23, and newly added Claims 24-41, are being acted upon.

4. The declaration stands objected to because it claims priority to Provisional Application No. 60/097,864. Applicant presumably intends to claim priority to Provisional Application No. 60/097,846 as indicated in the first line of the specification. A new declaration is required.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 17-19, 21-23, and newly added Claims 24-29, 33, 37, and 41 stand/are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed, for the reasons of record as set forth in the papers mailed 7/05/01, 1/09/02, 8/26/02, and 9/25/03, specifically, the recitation of a method for treating "neurogenic inflammation". This is a new matter rejection.

Applicant's arguments, filed 3/25/04 and 6/03/04, have been fully considered but they are not persuasive. Applicant argues that while the specification does not recite the term "neurogenic inflammation", never the less, the term is adequately disclosed.

Applicant argues that the Examiner has dismissed the teachings of the specification and the declaration of Dr. Martin Aquadro. Applicant cites both *Webster's Collegiate Dictionary* and *Stedmen's Medical Dictionary*.

Applicant is advised that the neither the teachings of the specification nor the declaration of Dr. Aquadro have been dismissed; Applicant's arguments and the declaration of Dr. Aquadro have not been found persuasive. It remains the Examiner's position that the disclosure does not support the invention as it is now claimed. For example, the disclosure of "the component of the inflammatory response...which is mediated by neural reflex mechanisms" (page 6 of the specification) or "rapid phase inflammatory responses...under neural regulation" (page 8 of the specification), is narrower in scope than the generic "neurogenic inflammation" of the instant claims.

Regarding Applicant's argument that *Webster's Collegiate Dictionary* defines "may" as "having the ability to" or have power, am able", a review of the reference shows that Applicant has chosen a definition that the reference teaches as being "archaic". Indeed, the definition of "may" that fits best in the instant context would be a "possibility or probability".

Regarding Applicant's argument regarding the use of *Stedmen's Medical Dictionary* to define neurogenic, Applicant argues, "the proper inquiry" is whether the specification "conveys to the skilled artisan that inflammation treatable by administration of a chemodenervating agent includes that inflammation that originates in, starts from or is caused by the central nervous system or nerve cells (nerve impulses)".

Note Applicant's argument that the inflammation of the specification "includes" neurogenic inflammation. It is this subgenus of inflammation now recited in the claims that the broader inflammation disclosed in the specification cannot support.

In the remarks of 6/03/04, Applicant further argues that a number of newly provided references support Applicant's argument that injury to a nerve cell results in an inflammatory cascade that involves mast cells that further propagate the neurogenic inflammatory cascade.

Applicant's arguments and references seem to best support the Examiner's position that neurogenic inflammation is at best a subgenus of inflammation. For example, Monteforte et al. (2001),

cited by Applicant, teaches mast cells "are best known for their involvement in...various inflammatory conditions...as well as neurogenic inflammation", clearly demonstrating that the author does not consider "neurogenic inflammation" and "inflammation" interchangeable terms.

Accordingly, it remains the Examiner's position that the specification cannot support claims amended to recite a method of treating neurogenic inflammation.

7. Claims 3 and 30-33 stand/are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method of reducing allergy induced conjunctivitis in a mouse comprising administering a botulinum toxin,

does not reasonably provide enablement for:

A) a method of reducing inflammation without causing muscle weakness,

for the reasons of record as set forth in the papers mailed 7/05/01, 1/09/02, 8/26/02, and 9/25/03.

Applicant's arguments, filed 3/25/04 and 6/03/04, have been fully considered but they are not persuasive. Applicant again asserts that the specification enables the method of the clams and argues, "The Examiner must accept a specification that teaches a skilled artisan how to use the claimed invention as being in compliance with the enablement requirement of § 112, unless there are reasons to doubt the objective truth of the statements relied upon to establish enablement" and cites MPEP 2164.02 and 2164.04.

MPEP 2164.03 states that most physiological activity is considered to involve unpredictable factors, thus, more than a single enabled species may be required. In the instant case, *no* enabled species of the claimed method are disclosed. As set forth previously, the specification simply does not disclose that muscle weakness was ever measured. Reduced inflammation was noted only as a side effect of treatment for other disorders. Accordingly, claims drawn to reducing inflammation without causing muscle weakness, assertedly due to a new (and previously unknown) "bioeffect", must be considered to be inherently unpredictable and requiring of some sort of enablement in addition to mere assertion.

Applicant makes a number of assertions regarding the examples and teachings of the specification, apparently in an argument that the specification and examples taken together

support the invention of the instant claims.

First note that a number of the assertions are factually incorrect. For example, Applicant asserts, "The specification also teaches doses above 2.5 botulinum units that are many fold lower than the dose required to treat movement disorders. (*See*, above; especially page 4, paragraph 2 and page 19, paragraph 1)." What the specification actually discloses is, "the dosage associated with such regional movement diseases is on the order of 25-600 units" (page 4) and "Minimum doses range between 0.6 units to 15 units and are far lower than that required to produce regional weakness" (page 20). Applicant asserts that, "the specification provides 14 pages of examples... examples and tests that are not limited to the treatment of conjunctivitis." A review of the "examples" discloses: a case study of a woman treated for involuntary facial movements in which vasodilation, erythema and edema were blocked; a case study in which regional facial flushing was blocked as a result of treatment for glabelar lines; a conjunctivitis experiment in which erythema, edema, and scratching were reduced; four blepharoconjunctivitis patients in which irritation, itching, erythema and general discomfort were improved; twenty blepharospasm patients in which photophobia was mitigated; and four torticollis patients in which red patches were reduced. For *none* of these patients was it disclosed that the doses of Botox™ employed were sufficient to reduce inflammation but below that necessary to cause substantial muscle weakness. Indeed, in most of these cases it appears that Botox™ was employed in a method *intended* to cause muscle weakness and an anti-inflammatory side effect was observed. Regarding the rheumatoid arthritis and internal inflammation "examples", the specification merely asserts that the claimed method can be used to treat these conditions.

8. The instant application claims the benefit of priority to Provisional Application No. 60/097,864. Applicant presumably intends to claim priority to Provisional Application No. 60/097,846. The benefit of priority is denied because the '846 application does not teach a method for treating neurogenic inflammation or gout, nor a method comprising a first step of identifying a subject suffering from an inflammatory condition/blepharoconjunctivitis, classic type 1 hypersensitivity/neurogenic inflammation. The priority date of the instant claims is the filing date of the instant application, 8/25/99.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

10. Claims 1, 5-6, and 17-29, 34, 37, 38, and 41 stand/are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,063,768 (filed 9/04/97), for the reasons of record as set forth previously.

Applicant has requested that an interference be declared between the instant claims and the claims of the '768 patent.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1, 5-8, 10-12, 17-29, and 34-41 stand/are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,063,768 (filed 9/04/97)) in view of The Merck Manual (1992) for the reasons of record as set forth previously.

Applicant has requested that an interference be declared between the instant claims and the claims of the '768 patent.

13. The following are new grounds for rejection.

14. Claims 1, 3, 5-8, 10-12, 17-19, 21-23, and newly added Claims 24-41 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) A method comprising a first step of identifying a subject suffering from an inflammatory condition/ blepharoconjunctivitis/classic type 1 hypersensitivity/neurogenic inflammation(Claims 1, 10, 11, and 24).

B) A method comprising blocking nerve and mast cell release of preformed mediators that produce permeability (Claims 19 and 26).

C) A method comprising administering botulinum toxin in a dose that is lower than that necessary to produce regional muscle weakness (Claims 30-33).

D) A method wherein the botulinum toxin dose is between 2 and 60 units (Clams 34-37).

Regarding A), the specification does not disclose this identifying step.

Regarding B), the specification discloses only increased permeability.

Regarding C), the specification discloses only substantial muscle weakness.

Regarding D), the specification does not disclose this range of dosages.

15. Claims 1, 5, 34, and 38 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by U.S. Patent No. 5,437,291.

The '291 patent teaches a method of identifying and treating a patient suffering from an inflammatory disorder (anal fissures or hemorrhoids) comprising administering a therapeutically effective dose of botulinum toxin A to an effected area wherein the dose of botulinum toxin A reduces inflammation (see particularly the Abstract and Table 1). The reference additionally teaches a dosage of 0.1 to 1000 units (see particularly column 5).

The reference clearly anticipates the claimed invention.

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

18. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

1/19/05

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